

Emergence and Transmission Dynamics of SARS-CoV-2 During Early Stages of COVID-19 pandemic in Wisconsin

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BACKGROUND

COVID-19 was declared a pandemic by the WHO on March 11, 2020, followed by a national emergency in the US on March 13, 2020. As of mid-April 2021, Wisconsin has ~650K cases with 113K cases from Milwaukee. The City of Milwaukee Health Department Laboratory (MHDL) has played pivotal role by detecting COVID19 cases within 24 hours of specimen collection from city and surrounding communities (Table 1). Initial studies suggested SARS-CoV-2 transmission mainly via droplets and close contact with infected pre-symptomatic (or asymptomatic) and symptomatic cases. To understand transmission patterns in local community and minimize the spread of new SARS-CoV-2 clusters, active genomic surveillance was initiated. Rapid whole genomic sequencing and phylogenetic analysis at University of Wisconsin, AIDS Vaccine Research Laboratory (AVRL) and MHDL revealed community transmission and fewer introductions as compared to surrounding communities. Real time genomic surveillance can play important role to guide to develop effective public health and infection prevention measures to prevent community transmission, besides monitoring evolution of SARS-CoV-2.

Figure 1: Number of sequenced COVID samples by ZIP code from the Milwaukee County patients in month of March and April, 2020.

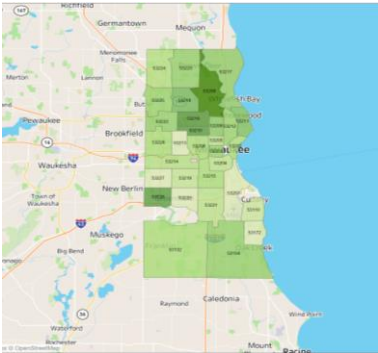


Table 1: Overall Milwaukee County COVID-19 Summary Statistics (Mar 5 – May 5, 2020)

Number of tests 19,081
Number of cases 3,390
Percentage of positive tests 17.8%

Number of hospitalizations 1,785
Number of deaths 203
Case fatality rate 6.0

METHODS

A subset of SARS-CoV-2 positive specimens in March- April 2020 from Milwaukee (#97) and other neighboring cities (#66) were sequenced. Selection was based on isolates from hot spots (Figure 1), LTCF, jails, travel associations, households, and outbreaks. RNA extracts were SARS-CoV-2 positive clinical samples using CDC 2019 Novel Coronavirus (2019-nCoV) Real-Time Reverse Transcriptase (RT)-PCR Diagnostic Panel. RNA extracts with Ct value ≤30 were used at AVRL per modified ARTIC protocol using MinION (Oxford Nanopore) (<https://www.nature.com/articles/s41467-020-19346-z>). Consensus sequences were derived using a modified ARTIC bioinformatics protocol (<https://artic.network/ncov-2019/ncov-2019-bioinformatics-sop.html>) and were shared on Global Initiative on Sharing All Influenza Data (GISAID). A time-resolved phylogenetic tree was built, and clades assigned using Nextstrain tools and nomenclature. Fig 2 shows hierarchical relationship among various nextstrain clades.



Figure 2 Schematic showing hierarchical relationships among Nextstrain clades (<https://nextstrain.org/blog/2021-01-06-updated-SARS-CoV-2-clade-naming>)

RESULTS

Local transmission in Milwaukee County beginning early March lead to large numbers of the COVID-19 cases (Table 1). In late March and early April, multiple introductions of SARS-CoV-2 detected into Milwaukee County, likely Asian-origin, resulting in large local epidemic with widespread community transmission (Figure 3A). In Milwaukee, SARS-CoV-2 mostly found to be clustered closely, consistent with fewer introductions and subsequent community transmission in comparison to Madison Dane County, Wisconsin (Figure 3B). Most common clades found in Milwaukee county included 19A (n = 104, 57.1%) followed by 20C clade (n = 62, 34.1%), 19B, 20B, and 20A compared to Dane county clades 19B, 20A, and 20C (Figure 4).

Figure 4. Milwaukee county vs Dane County, WI: SARS-CoV-2 Genomes sampled between March and April 2020

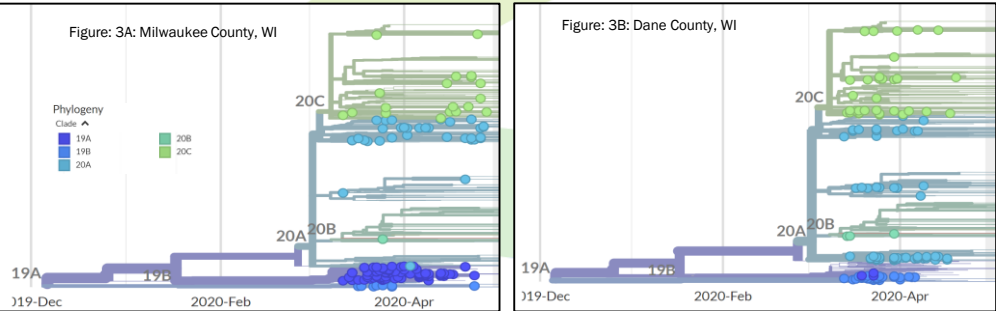


Figure 3: A time-resolved phylogenetic tree built using Nextstrain tools for 131 samples collected in Milwaukee county (A) and 182 samples collected in Dane county (B). Clade is denoted by color where dark blue denotes 19A, blue 19B, aqua 20A, green 20B, and yellow green 20C.

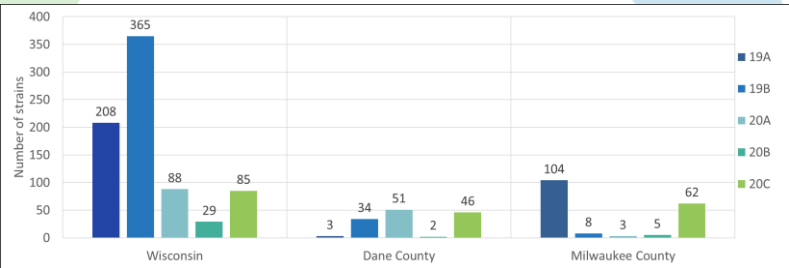


Figure 4: Prevalence and frequency of different nextstrain clades (19A, 19B, 20A, 20B, and 20C) in two demographically and geographically different counties in state of Wisconsin (March - April, 2020). Data source: Nextstrain and GISAID open data sources.

DISCUSSION

1. Genomic epidemiology contributes to not only identification of circulating patterns based on lineage/clade assignments, but also help trace local transmission chains, temporal and geographical evolution of virus in relation to epidemiological data and measures implemented to contain local outbreaks
2. Aggressive testing and timely genomic sequencing aids in cluster detection, case investigations, and contact tracing in LTCF, other congregate living settings (group homes and homeless shelters, correctional facilities, and multi-family households)
3. Development of robust genomic surveillance at local and national level for timely public health response needs sustained lab capacity and resources to monitor and control spread of SARS-CoV-2 and guidance and coordination from scientific community.
4. As variants continue to emerge as the pandemic unfolds, the best chance of minimizing their frequency and impact will be to continue public health measures that reduce transmission; includes mask mandates, social distancing requirements, limited gatherings, and mass vaccinations.

CONCLUSION

The preliminary results indicated that expanded detection capabilities and whole genome sequencing efforts at a local level will aid not only to isolate and contain SARS-CoV-2 cases but limit the establishment of new transmission clusters. Near real-time sequencing and data analysis will also enable public health jurisdictions to identify emerging variants of SARS-CoV-2 for further characterization by the scientific community or researchers. Partnership with academic centers, industry, non-governmental organizations, and public health agencies is needed to accomplish this task of real-time genomic surveillance to prevent emergence and spread of highly transmissible variants in future.

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